

REMARKS

The issues outstanding in the Office Action mailed May 9, 2008, are the rejections under 35 USC 112, 102, 103. Reconsideration of these issues, in view of the following discussion, is respectfully requested.

Rejection under 35 USC 112

Claim 4, 5, 7-11 have been rejected under 35 USC 112, first paragraph, as failing to comply with the written description requirement. Reconsideration of each of these rejections is respectfully.

It is argued at page 3 that the recitation that the material is decellularized “until essentially no residual cell nuclei are observed on microscopic examination of the tissue” does not find support in the specification. This is respectfully submitted no to be the case. It is well known that “decellularization” in a manner which would enable tissue to be used in an implant must remove all cellular materials so as to avoid immunogenicity. This is clearly explained in the specification at pages 1 through 4. Moreover, the specification discusses “complete decellularization” as being necessary, and teaches that such is achieved the present method, see also page 12, paragraph 24 of the specification. It is well accepted that for written description, “*ipsis verbis*” support is not necessary. That is, the exact words recited in claims need not also be found in the specification, if the specific concept embodied in the words is taught to have invented by the inventors. See for example, *In re Wertheim et al.*, 541 F.2d257, 191 U.S.P.Q. 90 (CCPA 1976). Thus, the above noted discussion in the specification clearly teaches to one of ordinary skill in the art that the present invention involves decellularization until no residual cell nuclei are observed on microscopic examination. However, in order to expedite prosecution, independent claim 10 has been amended in order to recites specific conditions which result in such complete decellularization. Moreover, new independent claim 12 has been added which recites “complete decellularization” of the tissue, this recitation being suggested in the

specification as discussed above. It is submitted that these claims fully satisfy 35 USC 112, and withdrawal of the rejection is respectfully requested.

Rejection Under 35 USC 102(b)

Claims 5, 7-10 has been rejected under 35 USC 102(b) over newly cited Login '237. Reconsideration of this rejection is respectfully requested. Login discloses a process employing microwave irradiation along with a physiologic salt solution or a dilute aldehyde solution, to preserve tissue in the preparation of bioprosthesis for implantation into patient. In the method of Login et al., a specimen of biological tissue is immersed in an osmotically balanced solution (OBS). The purpose of utilizing OBS is to *prevent the loss* of important cellular constituents due to diffusion. See, col. 5, lines 9-11. This is consistent with "tissue fixing" e. g. by exposure to glutaraldehyde or formaldehyde, note the discussion of cell fixing at column 2, along 31-33 and lines 52-53 patent. Such "fixing" is *not* decellularization in a complete matter, so as remove all cells.

Treatment or immersion a solution such as osmotically balanced solution does not enable removal of cellular components, even with the microwave radiation treatment of the patent. In the Login's method, the tissue immersed in OBS initially at room temperature (approximately 20°C) is irradiated with microwave energy at a sufficient does and for a sufficient time such that the temperature of the solution is within the range of 35°C to 50°C. This time is short, e.g. between one and fifty seconds. See, e.g. claim 6.

In the present invention, the tissue immersed in the treating solution is irradiated with considerably greater intensity, e.g., with microwaves at a frequency of 2450MHz (the frequency of a standard microwave oven) for a net period of time so as to achieve complete decellularization (see Claim 12) or for at least 1 hour while maintaining the temperature in the range of 0°C to 40°C, (see Claim 10). The duration of microwave irradiation in Claim 10 is at least 72 times greater than the duration of microwave irradiation of Login's method.

Moreover, in Login, the microwave oven will be automatically shut off when the pre-set final irradiation temperature of the solution is obtained (col. 4, lines 65-67). In other words, Login never irradiates the tissue specimen in OBS with microwave energy at a does and for a

length of time such that temperature of the solution reaches above patentees' preset temperature of 35°C to 50°C. Such duration of microwave irradiation is not sufficient to achieve complete decellularization. With a large enough dose of microwave energy to remove cellular membrane and release intracellular components, such as in the present invention, it is necessary to cool the tissue in the treating solution to maintain the generating temperature from 0°C to 40°C as recited in the claims.

In short, the disclosure of Login is simply does not suggest to one of ordinary skill, much less disclose, complete decellularization and/or the conditions recited in the present invention. Login thus in no way anticipates the present claims, and withdrawal of the rejection respectfully requested.

Rejection Under 35 USC 102(b)

Claims 4 and 11 are rejected under 35 USC 103 over Login taken with Giberson and Boon. Reconsideration of this rejection is also respectfully requested. In Giberson a tissue specimen is immersed in a formalin based solution, is irradiated with microwaves. Formalin is well known as a fixation chemical of biological tissues for microscopic inspection. Since the morphological characteristics of the tissue specimen must be preserved for diagnostic purposes, Giberson does not remove any cellular component from the tissue. Boon teaches the use of alcohol or glutaraldehyde as an immersion fluid (page 7, lines 51-55) when irradiating tissue with microwaves. Thus, again only fixation is taught, and not complete decellularization. The secondary references accordingly do nothing to remedy the deficiencies of Login, and even in combination do not suggest the present claims. Withdrawal of this rejection is therefore respectfully requested.

Should the Examiner have any questions or comments, he or she is cordially invited to telephone the undersigned at the number below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Harry B. Shubin/

Harry B. Shubin, Reg. No. 32,004
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: AKA-0286
Date: November 10, 2008